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=> file casreact
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FILE CONTENT:1840 - 10 May 2009 VOL 150 ISS 20

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=> d que
L1                STR
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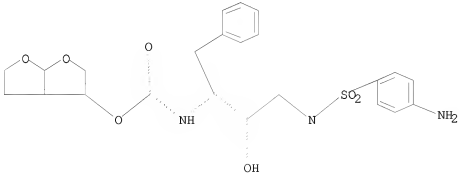


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Structure attributes must be viewed using STN Express query preparation.
L4             6 SEA FILE=CASREACT SSS FUL L1 (   221 REACTIONS)


=> d l4 1-6 ibib abs fcrd

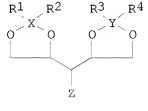

L4   ANSWER 1 OF 6  CASREACT  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         145:293291  CASREACT
TITLE:                    Process for the preparation of cyclic alditols for use
                          as protease inhibitors in the treatment of HIV
INVENTOR(S):              Linclau, Bruno
```

PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.
SOURCE: PCT Int. Appl., 45pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006089942	A1	20060831	WO 2006-EP60246	20060224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006217922	A1	20060831	AU 2006-217922	20060224
CA 2595295	A1	20060831	CA 2006-2595295	20060224
EP 1856125	A1	20071121	EP 2006-724879	20060224
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008531522	T	20080814	JP 2007-556615	20060224
IN 2007DN05992	A	20070817	IN 2007-DN5992	20070801
CN 101128469	A	20080220	CN 2006-80005852	20070823
MX 2007010378	A	20070925	MX 2007-10378	20070824
KR 2008005183	A	20080110	KR 2007-719729	20070829
NO 2007004880	A	20070925	NO 2007-4880	20070925
US 20090054668	A1	20090226	US 2008-816607	20080520

PRIORITY APPLN. INFO.: EP 2005-101462 20050225
US 2005-683699P 20050523
WO 2006-EP60246 20060224

OTHER SOURCE(S): MARPAT 145:293291
GI



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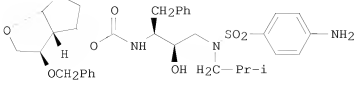
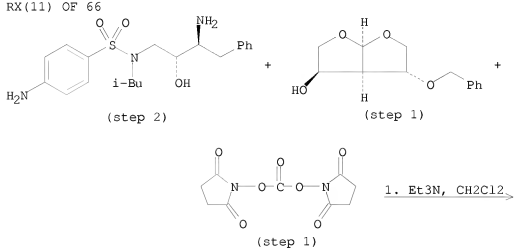


II

AB A process for the preparation of alditols, I, wherein X and Y are Si or C; R1-R4 are independently H or monovalent hydrocarbon radicals; Z is a formyl, hydroxymethyl or methylene group are useful intermediates for the preparation of cyclic alditols. Thus, II was prepared in 38% yield and tested as an HIV-antiviral agent (PEC50 between 5.7 and 8.8).

RX(11) OF 66



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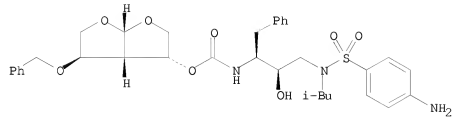


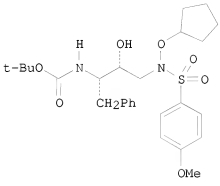
38%

CON: STAGE(1) 4 hours, room temperature
STAGE(2) overnight, room temperature

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:248118 CASREACT
TITLE: Synthesis and antiviral activities of novel N-alkoxy-arylsulfonamide-based HIV protease inhibitors
AUTHOR(S): Sherrill, Ronald G.; Furfine, Eric S.; Hazen, Richard J.; Miller, John F.; Reynolds, David J.; Sammond, Douglas M.; Spaltenstein, Andrew; Wheelan, Pat; Wright, Lois L.
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005),

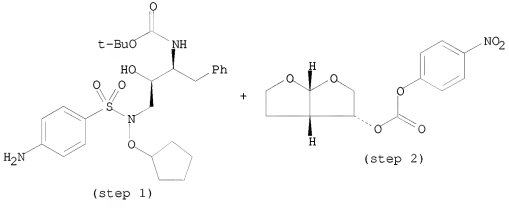
15(15), 3560-3564
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



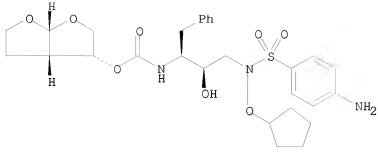
I

AB A series of N-alkoxy-arylsulfonamide HIV protease inhibitors, e.g., I, with low picomolar enzyme activity and single digit nanomolar antiviral activity is disclosed.

RX(26) OF 92



RX(26) OF 92



41%

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:133352 CASREACT
TITLE: Process for the preparation of (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl (1S,2R)-3-[[(4-aminophenyl)sulfonyl](isobutyl)amino]-1-benzyl-2-hydroxypropylcarbamate from 1-oxiranyl-2-phenylethylcarbamates.
INVENTOR(S): Goyvaerts, Nicolaas Martha Felix; Wigerinck, Piet Tom Bert Paul; Zinser, Hartmut Burghard; Ebert, Birgit M.
PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005063770	A1	20050714	WO 2004-EP53692	20041223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004309122	A1	20050714	AU 2004-309122	20041223
CA 2549460	A1	20050714	CA 2004-2549460	20041223
EP 1725566	A1	20061129	EP 2004-805020	20041223
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1898248	A	20070117	CN 2004-80038298	20041223
BR 2004017272	A	20070327	BR 2004-17272	20041223
JP 2007520468	T	20070726	JP 2006-546183	20041223

IN 2006DN02122	A	20070713	IN 2006-DN2122	20060419
KR 2006123740	A	20061204	KR 2006-709136	20060510
MX 2006007211	A	20060818	MX 2006-7211	20060622
US 20070060642	A1	20070315	US 2006-596732	20060622
PRIORITY APPLN. INFO.:			EP 2003-104949	20031223
			US 2004-568183P	20040504
			WO 2004-EP53692	20041223

OTHER SOURCE(S): MARPAT 143:133352

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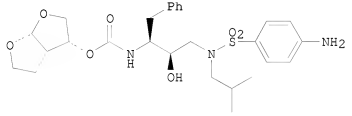

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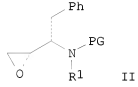
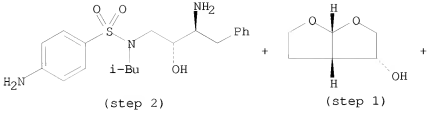
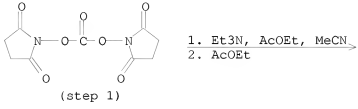


II

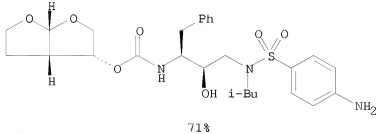
AB A process for the preparation of (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl (1S,2R)-3-[[(4-aminophenyl) sulfonyl](isobutyl) amino]-1-benzyl-2-hydroxypropylcarbamate (I) comprises introduction of an isobutylamino group into 1-oxiranyl-2-phenylethylcarbamates (II; R1 = H, alkyl; PG = protecting group) followed by introducing a p-nitrophenylsulfonyl group into the product of the first reaction, reduction of the nitro group, deprotection, and coupling of the product with a (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl derivative Thus, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol in EtOAc was treated sequentially with disuccinimidyl carbonate in MeCN, Et3N in EtOAc, 4-amino-N-[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]-N-(isobutyl)benzenesulfonamide (preparation given) in EtOAc, and aqueous MeNH2 in EtOH to give 71% I ethanolate.

RX(6) OF 14





RX(6) OF 14



71%

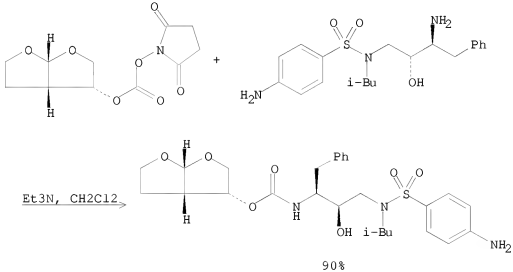
CON: STAGE(1) room temperature
STAGE(2) cooled

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:211389 CASREACT
TITLE: Discovery and Selection of TMC114, a Next Generation HIV-1 Protease Inhibitor
AUTHOR(S): Surleraux, Dominique L. N. G.; Tahri, Abdellah; Verschueren, Wim G.; Pille, Geert M. E.; de Kock, Herman A.; Jonckers, Tim H. M.; Peeters, Anik; De Meyer, Sandra; Azijn, Hilde; Pauwels, Rudi; de Bethune, Marie-Pierre; King, Nancy M.; Prabu-Jeyabalan, Moses; Schiffer, Celia A.; Wigerinck, Piet B. T. P.
CORPORATE SOURCE: Tibotec BVBA, Mechelen, B-2800, Belg.
SOURCE: Journal of Medicinal Chemistry (2005), 48(6), 1813-1822
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The screening of known HIV-1 protease inhibitors against a panel of multidrug-resistant viruses revealed the potent activity of TMC126 on

drug-resistant mutants. In comparison to amprenavir, the improved affinity of TMC126 is largely the result of one extra hydrogen bond to the backbone of the protein in the P2 pocket. Modification of the substitution pattern on the phenylsulfonamide P2' substituent of TMC126 created an interesting SAR, with the close analog TMC114 being found to have a similar antiviral activity against the mutant and the wild-type viruses. X-ray and thermodn. studies on both wild-type and mutant enzymes showed an extremely high enthalpy driven affinity of TMC114 for HIV-1 protease. In vitro selection of mutants resistant to TMC114 starting from wild-type virus proved to be extremely difficult; this was not the case for other close analogs. Therefore, the extra H-bond to the backbone in the P2 pocket cannot be the only explanation for the interesting antiviral profile of TMC114. Absorption studies in animals indicated that TMC114 has pharmacokinetic properties comparable to currently approved HIV-1 protease inhibitors.

RX(11) OF 179



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REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 142:56210 CASREACT

TITLE: Stereoselective Photochemical 1,3-Dioxolane Addition to 5-Alkoxymethyl-2(5H)-furanone: Synthesis of Bis-tetrahydrofuranyl Ligand for HIV Protease Inhibitor UIC-94017 (TMC-114)

AUTHOR(S): Ghosh, Arun K.; Leshchenko, Sofiya; Noetzel, Marcus

CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA

SOURCE: Journal of Organic Chemistry (2004), 69(23), 7822-7829 CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

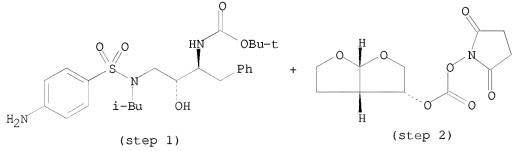
LANGUAGE: English

GI

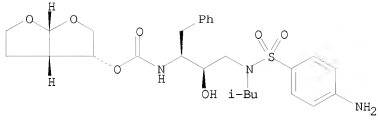
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB HIV protease inhibitor UIC-94017 I is prepared using the stereoselective photochem. addition of 1,3-dioxolane to nonracemic 5-substituted 2-furanones to yield dioxolanylfuranones as the key step. Nonracemic 5-(benzyloxymethyl)-2-furanone II (R = PhCH2) is prepared in 4-7 steps from benzyloxyacetaldehyde using a lipase-mediated resolution to generate the desired absolute stereochem. Addition of vinylmagnesium bromide to benzyloxyacetaldehyde yields 1-(benzyloxy)-3-buten-2-ol which undergoes enantioselective acylation with isopropenyl acetate in the presence of lipase PS-30 to yield (S)-1-(benzyloxy)-3-buten-2-ol in 49% yield and 99% ee and (R)-1-(benzyloxy)-3-buten-2-ol acetate in 49% yield (which can be converted to the desired alc. in 3 steps and 82% yield and 81% ee). Acylation of (S)-1-(benzyloxy)-3-buten-2-ol with acryloyl chloride followed by ring closure with the 2nd generation Grubbs ruthenium metathesis catalyst provides II (R = PhCH2). II [R = Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] are also prepared by a three-step procedure from isopropylidene-D-glycerol. Irradiation of II [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] and 1,3-dioxolane in the presence of benzophenone yields dioxolanylfuranones III [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] in 36-93% yields and with 76:24-97:3 selectivity for the trans stereoisomers (in all but one case ≥96:4 stereoselectivity). Reductive cleavage of the benzyl group of III (R = PhCH2), lithium aluminum hydride reduction of the lactone and acid-mediated cyclization yields the alc. epimer of desired hexahydrofurofuranol IV; either oxidation of the alc. to the ketone followed by reduction or Mitsunobu inversion followed by hydrolysis of the p-nitrobenzoate ester yields IV stereoselectively. Ring opening of (S,S)-N-Boc-α-benzyloxiranemethanamine with isobutylamine followed by sulfonylation of the secondary amine with p-nitrobenzenesulfonyl chloride yields intermediate carbamate V. Reduction of the nitro group of V, removal of the Boc group, and coupling with the N-hydroxysuccinimidyl carbonate mixed ester of IV yields I.

RX(30) OF 315



RX(30) OF 315



89%

CON: STAGE(1) 40 minutes, 23 deg C
STAGE(2) 3 hours, 23 deg C

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:339141 CASREACT

TITLE: Novel arylsulfonamides possessing sub-picomolar HIV protease activities and potent anti-HIV activity against wild-type and drug-resistant viral strains

AUTHOR(S): Miller, John F.; Furfine, Eric S.; Hanlon, Mary H.; Hazen, Richard J.; Ray, John A.; Robinson, Laurence; Samano, Vicente; Spaltenstein, Andrew

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

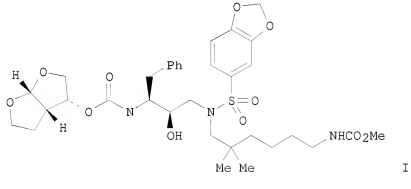
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(4), 959-963
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

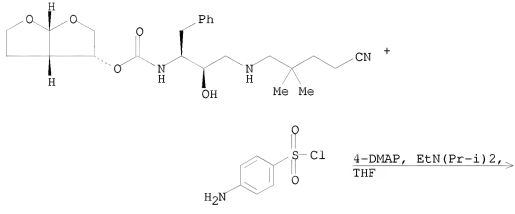


I

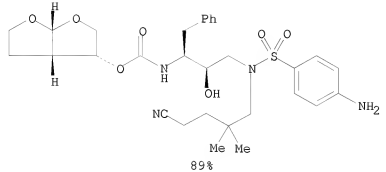
AB Furanofuryl analogs of the HIV protease inhibitor amprenavir such as I are prepared in which a terminally substituted n-alkyl group is appended to the N-iso-Bu group of amprenavir and in which the substituents on the N-arylsulfonyl moiety are varied. Some of the inhibitors such as I are found to have greatly enhanced inhibition of HIV protease; the amprenavir analogs also inhibit the growth of both wild-type and resistant strains of

HIV and are more effective against the HIV strains than the currently marketed HIV protease inhibitors amprenavir, indinavir, and nelfinavir. E.g., I inhibits wild-type HIV protease with a Ki value of 0.014 pM, and inhibits wild-type and resistant strains of HIV with IC50 values of between 1.6 nM and 15 nM.

RX(10) OF 284



RX(10) OF 284



89%

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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